BC Cancer Protocol Summary for Therapy for Non-Metastatic Castration Resistant Prostate Cancer Using Enzalutamide

Protocol Code: *UGUNMPENZ*

Tumour Group: *Genitourinary*

Contact Physician: *Dr. Christian Kollmannsberger*

ELIGIBILITY:

Patients must have:

- Non-metastatic castration resistant prostate cancer (nmCRPC),
  - No radiologic evidence of metastases (negative bone scan, negative CT of pelvis, abdomen, chest) within the last 6 months (exception: pelvic lymph nodes < 2 cm in short axis below the aortic bifurcation)
- No prior chemotherapy for nmCRPC,
- PSA doubling time of less or equal to 10 months, and
- A BC Cancer "Compassionate Access Program" (CAP) request must be approved prior to treatment

Patients should have:

- ECOG performance status 0 to 2

Notes:

- Patients with nmCRPC are eligible to receive any of the following, but not their sequential use:
  - apalutamide (UGUPAPA),
  - darolutamide (UGUNMPDAR), or
  - enzalutamide (UGUNMPENZ)
- Patients who have progressed to metastatic disease on enzalutamide (UGUNMPENZ):
- Are eligible to receive all of the following:
  - DOCEtaxel (GUPDOC),
  - cabazitaxel (GUPCABA), and
  - radium in metastatic CRPC (GUPRAD)
- Are **NOT** eligible to receive enzalutamide (UGUPENZ) or abiraterone (UGUPABI, UGUPAVOABI, UGUPAVNABI)

EXCLUSIONS:

Patients must not have:

- Metastatic prostate cancer (exception: pelvic lymph nodes < 2 cm in short axis below the aortic bifurcation)
- Prior treatment with apalutamide (UGUPAPA) or darolutamide (UGUNMDAR) in nmCRPC
- Prior chemotherapy for nmCRPC
- Uncontrolled hypertension (systolic blood pressure greater than 160 mmHg or diastolic greater than 95 mmHg)

TESTS:

- Baseline: CBC & Diff, creatinine, sodium, potassium, PSA, testosterone, blood pressure
- Baseline if clinically indicated: ECG
- Each time seen by physician: PSA, blood pressure
- If clinically indicated: creatinine, sodium, potassium, testosterone, ECG

TREATMENT

Drug	Dose	BCCA Administration Guideline
enzalutamide	160 mg daily	PO

One cycle consists of 4 weeks (30 days) of enzalutamide. Dispense a 90 day supply with each physician visit. Treat until disease progression or unacceptable toxicity.

Dose reduction:
Dose level -1: enzalutamide120 mg PO daily
Dose level -2: enzalutamide 80 mg PO daily

Androgen ablative therapy (e.g., LHRH agonist, LHRH antagonist) should be maintained. Discontinue other antiandrogen (e.g., bicalutamide), if used as part of combined androgen blockade.

PRECAUTIONS:

1. **QT prolongation:** Enzalutamide is associated with QTc prolongation. It should be used with caution in patients with a known history of QT prolongation, risk factors for torsade de pointes (e.g. hypokalemia) or patients who are taking medications known to prolong the QT interval.
2. **Seizure:** Enzalutamide is associated with an increased risk of seizure, with a greater risk of seizure at daily doses higher than 160 mg. Seizures resolved after treatment cessation.
3. **Hypertension:** Enzalutamide is associated with increased blood pressure in approximately 7% of patients. Hypertension rarely leads to discontinuation or dose modification, but may require antihypertensive treatment. Blood pressure will need to be monitored once every 2 weeks for the first three months of enzalutamide therapy. Temporary suspension of enzalutamide is recommended for patients with severe hypertension (greater than 200 mmHg systolic or greater than 110 mmHg diastolic). Treatment with enzalutamide may be resumed once hypertension is controlled.
4. **Drug interactions**: CYP2C8 inhibitors (e.g. gemfibrozil) may increase the serum level of enzalutamide. Consider reducing enzalutamide to 120 mg or 80 mg once daily in patients who must be co-administered with a strong CYP2C8 inhibitor.

Call Dr. Christian Kollmannsberger or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Sternberg CN, Fizazi K, Saad F, et at. Enzalutamide and Survival in Nonmetastatic Castration-Resistant Prostate Cancer. N Engl J Med. 2020;382:2197-206
2. Hussain M, Fizazi K, Saad F, et al. Enzalutamide in Men with Nonmetastatic, Castration-Resistant Prostate Cancer. N Engl J Med. 2018; 378:2465-74